

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
13 May 2004 (13.05.2004)

PCT

(10) International Publication Number
WO 2004/039957 A3

- (51) International Patent Classification⁷: **A61K 48/00**, C07H 21/04, C12Q 1/68
- (21) International Application Number: PCT/US2003/034424
- (22) International Filing Date: 29 October 2003 (29.10.2003)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
60/422,419 29 October 2002 (29.10.2002) US
- (71) Applicant (for all designated States except US): **THE CENTER FOR BLOOD RESEARCH, INC.** [US/US]; 800 Huntington Avenue, Boston, MA 02115 (US).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): **LIEBERMAN**, Judy [US/US]; 63 Buckminster Road, Brookline, MA (US). **SHANKAR**, Premlata [—/US]; 46 Hilburn Street, Roslindale, MA 02131 (US). **NARASIMHASWAMY**, Manjunath [—/US]; 46 Hilburn Street, Roslindale, MA 02131 (US). **SONG**, Erwei [—/US]; 11 Monument Way, Quincy, MA (US). **LEE**, Sang-Kyung [—/US]; 175 Freeman St. #402, Brookline, MA 02446 (US).
- (74) Agent: **RESNICK**, David S.; Nixon Peabody LLP, 100 Summer Street, Boston, MA 02110-2131 (US).
- (81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- Published:**
— with international search report
— before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments
- (88) Date of publication of the international search report:
30 September 2004
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: INHIBITION OF GENE EXPRESSION USING RNA INTERFERING AGENTS

(57) Abstract: The present invention is based, at least in part, on the discovery of compositions and methods for the treatment and prevention of infectious diseases or disorders, e.g., HIV infection, AIDS, and AIDS-related diseases. In particular, the present invention pertains to methods of modulating cellular gene expression or protein activity, e.g., CCR5, gene expression or protein activity and/or gene expression or protein activity of a gene or sequence of an infectious agent, in order to treat or prevent infectious diseases or disorders, HIV infection, AIDS, or an AIDS-related disease or disorder. In one embodiment, the combination of an RNA interfering agent targeting a cellular gene in combination with an RNA interfering agent targeting a gene or sequence of an infectious agent results in prolonged prevention of infection by an infectious agent. The present invention is based on the identification of novel RNA interference agents, e.g., siRNA molecules, which target cellular genes, e.g., chemokine receptors, e.g., the CCR5 gene, and result in inhibition of target gene expression on target gene expressing cells, thereby inhibiting entry of infectious agents, e.g., HIV infection into target cells, prevention infection, and/or suppressing replication in established infection.

BEST AVAILABLE COPY

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/34424

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61K 48/00; C07H 21/04; C12Q 1/68
US CL : 514/44; 435/6, 91.1, 325, 375; 536/23.1, 24.5

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 514/44; 435/6, 91.1, 325, 375; 536/23.1, 24.5

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Medline, CA, SciSearch, Biosis, West, Embase

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	MARTINEZ et al. Suppression of Chemokine Receptor Expression by RNA Interference	22-29, 34-36, 44-58
---	Allows for Inhibition of HIV-1 Replication. AIDS, 2002, Vol. 16, pages 2385-2390,	-----
Y	entire document.	1-7, 10-21, 30-33, 37-43, and 59-61

☐

Further documents are listed in the continuation of Box C.

☐

See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T"

later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X"

document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y"

document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&"

document member of the same patent family

Date of the actual completion of the international search

08 August 2004 (08.08.2004)

Date of mailing of the international search report

26 AUG 2004

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Facsimile No. (703) 872-9306

Authorized officer

J. D. Schultz, Ph.D.

Telephone No. 571-272-1600

J. Roberts for

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/34424

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claim Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☒ Claim Nos.: 8 and 9
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐
☐

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.